Page 37, first full paragraph

Expression of Ikbkap was examined using both mouse embryo and adult mouse multiple tissue Northern blots (Clontech). The blots were probed with a 1045-bp PCR fragment that contains exons 2 through 11, which was generated using primer 1 (5' – GGCGTCGTAGAAATTGC-3') (SEQ ID NO: 87) and primer 2 (5' – GTGGTGCTGAAGGGGCAGGC-3') (SEQ ID NO: 88). The probe was radiolabeled (Sambrook et al., 1989) and was hybridized according to the manufacturer's instructions.

REMARKS

The specification has been amended to include sequence identifiers. The amended portions of the specification are reproduced in the Appendix attached hereto, with changes indicated. No new matter is introduced by the amendments and Applicants respectfully request entry thereof.

Respectfully submitted,
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APPENDIX

Amendments to the specification, showing [deletions] and additions made (in bold type).

Page 5, second full paragraph

In another embodiment, DNA is amplified using the following oligonucleotide primers: 5'- GCCAGTGTTTTTGCCTGAG – 3' **(SEQ ID NO: 82)**; 5'- CGGATTGTCACTGTTGTGC- 3' **(SEQ ID NO: 83)**; 5'- GACTGCTCTCATAGCATCGC- 3' **(SEQ ID NO: 84)**. In another embodiment, the assessing step further comprises an allele-specific oligonucleotide hybridization assay. In another embodiment, the allele-specific oligonucleotide hybridization assay is accomplished using the following oligonucleotides: 5'- AAGTAAG(T/C)GCCATTG- 3' **(SEQ ID NO: 85)** and 5'- GGTTCAC(G/C)GATTGTC **(SEQ ID NO: 86)**. In yet another embodiment, neuronal tissue from an individual is screened for the presence of truncated IKBKAP mRNA or peptides, wherein the presence of said truncated mRNA or peptides indicates that said individual possesses the FD1 and/or FD2 mutation in the IKBKAP gene.

Pages 8-9, description of Figures 6-11

Figure 6. The genomic sequence for *IKBKAP* **(SEQ ID NO: 1).**

Figure 7- The cDNA sequence for *IKBKAP* **(SEQ ID NO: 2).**

Figure 8- the amino acid sequence of the *IKBKAP* gene **(SEQ ID NO: 3).**

Figure 9- Comparison of the amino acid sequence of Ikap across several species **(SEQ ID NOS 4-9, respectively, in order of appearance).** Alignment of the amino acid sequence of Ikap (M_musculus) with that of *Homo sapiens* (H_sapiens), *Drosophila melanogaster* (D_melanogaster), *Saccharomyces cerevisiae* (S_cervisiae), *Arabidopsis thaliana* (A_thaliana), and *Caenorhabditis elegans* (C_elegans).

Figure 10- Comparison of the Novel Mouse *Ikbkap* Gene with Multiple Species Homologs

Figure 11- Mouse *Ikbkap* Exon and Intron Boundaries **(Acceptor site sequences have been assigned SEQ ID NOS 10-45, respectively, in order of appearance. Donor site sequences have been assigned SEQ ID NOS 46-81, respectively, in order of appearance).**

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Exon trapping experiments of cosmids from a physical map of the candidate region yielded 5 exons that were used to screen a human frontal cortex cDNA library. Several cDNA clones were isolated and assembled into a novel transcript encoding a 1332 AA protein that was later identified as *IKBKAP* (Cohen et al. 1998). The complete 5.9 kb cDNA sequence of *IKBKAP* has been submitted to GenBank under accession number AF153419. In order to screen for mutations in FD patients, total lymphoblast RNA was reverse transcribed and overlapping sections of *IKBKAP* were amplified by PCR and sequenced. Evaluation of

the splicing defect was performed using the following primers: 18F: GCCAGTGTTTTTGCCTGAG **(SEQ ID NO: 82)**; 19F: CGGATTGTCACTGTTGTGC **(SEQ ID NO: 83);** 23R: GACTGCTCTCATAGCATCGC **(SEQ ID NO: 84)** (Fig. 1).

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In a preferred embodiment, the amplification primers used for detecting the T-C mutation and the G-C mutation in the FD gene are 5'- GCCAGTGTTTTTGCCTGAG – 3' **(SEQ ID NO: 82)** / 5'-GACTGCTCTCATAGCATCGC- 3' **(SEQ ID NO: 84)** and 5'-CGGATTGTCACTGTTGTGC- 3' **(SEQ ID NO: 83)** / 5'-GACTGCTCTCATAGCATCGC-3, **(SEQ ID NO: 84)** respectively.

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Following PCR amplification, the PCR products are subjected to a hybridization assay using allele-specific oligonucleotides. In a preferred embodiment, the allele-specific oligonucleotides used to detect the mutatons in the FD gene are as follows:

5'- AAGTAAG(T/C)GCCATTG- 3' **(SEQ ID NO: 85)** and 5'-GGTTCAC(G/C)GATTGTC **(SEQ ID NO: 86).**

Page 37, first full paragraph

Expression of Ikbkap was examined using both mouse embryo and adult mouse multiple tissue Northern blots (Clontech). The blots were probed with a 1045-bp PCR fragment that contains exons 2 through 11, which was generated using primer 1 (5' – GGCGTCGTAGAAATTGC-3') **(SEQ ID NO: 87)** and primer 2 (5' – GTGGTGCTGAAGGGGCAGGC-3') **(SEQ ID NO: 88).** The probe was radiolabeled (Sambrook et al., 1989) and was hybridized according to the manufacturer's instructions.